Citation:

Seierstad SL, Seljeflot I, Johansen O, Hansen R, Haugen M, Rosenlund G, Frøyland L, Arnesen H. Dietary intake of differently fed salmon; the influence on markers of human atherosclerosis. Eur J Clin Invest. 2005 Jan;35(1):52-9.

PubMed ID: 15638820

Study Design:

Randomized controlled trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to investigate the effect of dietary intake of Atlantic salmon, fed on different fatty acid sources (fatty acid fish oil only/fish oil+rapeseed oil/rapeseed oil only), on the serum lipid profile and on atherosclerotic activity, assessed as circulating levels of markers of vascular inflammation and peroxidation , in patients with coronary heart disease (CHD).

Inclusion Criteria:

- Age >18
- Patients with clinically stable, angiographically-verified CHD
- The Regional Ethics Committee approved the study protocol
- All included patients gave their written informed consent

Exclusion Criteria:

- Patients <18 years of age
- Patients with acute myocardial infarction within previous 3 months
- Patients with unstable angina
- Patients with severe uncontrolled heart failure
- Patients receiving systemic steroid therapy of on immunosuppressive drugs
- Patients known to be noncompliant to consume the fish meals

Description of Study Protocol:

RECRUITMENT: Recruitment methods, sites, selection, etc. was not addressed in this paper.

DESIGN: This study is a six week, double-blinded, three-arm, randomized controlled trial.

DIETARY INTAKE/DIETARY ASSESSMENT METHODOLOGY: Each patient was schedule to receive five fish meals comprising approximately 700g salmon per week for six weeks. Patients were instructed not to make any further change in their dietary habits, which were recorded using a standardized food frequency questionnaire.

BLINDING: This study was a double-blind, randomized dietary intervention study.

INTERVENTION: After a 4-week run-in period in which the participants were asked not to change their habitual diet, the study population was randomly allocated to one of three parallel groups consuming approximately 700g/week for 6 weeks of tailor-made Atlantic salmon.

- Group 1: 100% South-American fish oil,
- Group 2: 50% South-American fish oil/50% rapeseed oil,
- Group 3: 100% rapeseed oil. All fish feeds satisfied the minimum requirement for n-3 polyunsaturated fatty acids (PUFAs) in salmonids. Nutreco ARC (Stavanger, Norway) provided the fish fillets color coded and blinded for both the patients and the investigators.

STATISTICAL ANALYSIS:

- The primary outcome was the possible differences in changes between the intervention groups in markers of atherosclerotic activity during the study period.
- Sample size estimation was based on previous studies with supplementation of highly concentrated n-3 PUFAs (capsules) where convincing changes in fatty acid profiles were obtained. Sixty patients (20 per group) were needed to detect a statistically significant difference between the groups in serum triglycerides with a power of 80 and a two-sided α value of 0.05.
- For demographic variables mean values ± SD or proportions

were reported. Owing to skewed data distribution of several variables, all ofther variables are given as median and inter-quartile range.
- For categorical variables and frequency a chi-square test was used.
- For intragroup changes Wilcoxon's Rank Sum test was used.
- For all intergroup comparisons the Kruskall-Wallis test followed by the Mann-Whitney U-test were used.
- Differences between the groups at baseline were observed for several variables, and thus for comparisons of intergroup differences in changes from baseline relative changes were used.
- A two-sided P-value of less than 0.05 was considered statistically significant.

Data Collection Summary:

TIMING AND METHOD OF MEASUREMENTS:

- After screening, study patients were clinically examined and asked to abstain from taking commercial dietary supplements of marine fish oils during the study period. After a 4-week run-in period, in which participants were asked not to change their habitual diet, subjects were randomly assigned to one of three conditions.
- At the end of the six week study, participants' blood samples were drawn in fasting conditions between 0800 h and 1000 h. Serum and plasmas were prepared within 1 hour and kept frozen at -70 degrees Celsius for batch analysis of the variables. Serum lipids were analyzed by conventional enzymatic methods.
- Serum vitamin E was analyzed with a HPLC system (as described in prior research). Serum thiobarbituric acid reactive substances were analyzed by a colourimetric method.
- Oxidized LDL-cholesterol was determined in EDTA-plasma using an ELISA method.
- Vascular cell adhesion molecule-1, intercellular adhesion molecule-1, P-selectin, E-selectin, tumor necrosis factor α (TNFα) , Interleukin-6 and Interleukin-10 were analyzed with commercial ELISA methods and high-sensitivity C-reactive protein was determined by DRG Instruments. P-selectin was measured in citrated plasma; otherwise serum was used.

DEPENDENT VARIABLES (OUTCOMES): Markers of human

artherosclerosis including: (1) serum fatty acid profile, (2) serum lipoproteins and (3) markers of vascular inflammation

INDEPENDENT VARIABLES: Dietary intake of differently fed Atlantic salmon,including: (1) 100% fish oil, (2) 50% fish oil/50% rapeseed oil, or (3) 100% rapeseed oil.

Description of Actual Data Sample:

INITIAL N: 60

ATTRITION (FINAL N): 58 (50 males, 8 females). One patient was deemed ineligible after enroll and one was not adherent to the study protocol.

AGE: 46-75

ANTHROPOMETRICS: Groups 1 and 3 differed in BMI (p=0.014)

LOCATION: Norway (no specific information stated)

Summary of Results:

- The serum fatty acid profiles of the patients after the intervention mirrored those of the corresponding salmon fillets and the respective salmon feeds.
- Significant differences between the groups were obtained, especially for the levels of total n-3 PUFAs and the n-3/n-6 fatty acid ratio, which was markedly increased in the 100% fish oil group in contrast to the two other groups (p=0.02 for all).
- Significant reductions of serum triglycerides and of vascular cell adhesion molecule-1 and interlukin-6 were obtained in patients receiving the 100% fish oil diet compared with the two other groups (p<0.05 for all).

Author Conclusion:

Tailor-made Atlantic salmon fillets very high in n-3 PUFAs of marine origin seem to impose favorable biochemical changes in patients with CHD when compared to ingestion of fillets with intermediate (i.e.50%) and low (i.e. 0%) levels of marine n-3 PUFAs, when replaced by rapeseed oil.

Reviewer Comments:

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes